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C. Stefe

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Rudolf Eckardt et al.

GAU 1624
Examiner T. McKenzie

Serial No. 09/447,490

Filed on 11/23/99

For A PROCESS FOR PRODUCING CARBAMAZEPINE

Attorney's Docket 0691-018A

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Box Appeal
Hon. Commissioner of Patents and Trademarks
Washington DC 20231

Sir:

Enclosed herewith in triplicate is a copy of the Reply to the Examiner's Answer, the consideration of which is requested on this appeal.

Please note below the new address of the undersigned attorney

Respectfully submitted

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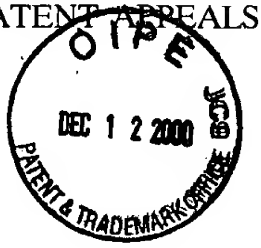
It is hereby certified that this is being mailed, as addressed above, on December 8, 2000

Cynthia A. Pilato

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES



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APPLICANTS' REPLY BRIEF

This replies to the Examiner's Answer (hereinafter "EA") in the above appeal, mail on December 1, 2000.

(A) Introduction

The repetitively disorganized and confusingly jumbled presentations and misrepresentations of the EA requires that the following be clearly understood before the necessity of plunging into a sequential reply to the EA.

(a) The EA is addressed to a process that is not the applicants'. The applicants' process is a single step process in which iminostilbene is reacted with an alkali cyanate salt in the presence of aqueous diluted or undiluted acetic acid to produce carbamazepine. The sole reference of record, Acklin et al., discloses a two-step process of: (i) reacting a cyanate salt with an acid that the reference specifies has to be a stronger acid than acetic acid, to form cyanic acid (i.e. hydrogen cyanide), then (ii) reacting the so formed hydrogen cyanide with iminostilbene to form carbamazepine.

(b) The applicants' single step in fact does not form any hydrogen cyanide, because that is a malodorous, poison gas (and was used as such in World War I), It was emphasized from the beginning in the disclosure of the application that hydrogen cyanide is evidently absent during the applicants' single step process which proceeds directly to the end product with a high yield.

(c) The EA attempts to shoehorn the 2-step process of the reference into the herein claimed single step process, because that is the only thing that the examiner appears to understand. In this attempt the EA employs spurious argumentation in the style of some academic dissertation, vaguely referring to some texts that were mentioned for the first time at this late stage in the introduction of the EA, and are not of record herein. However, it is well established under the law that patentability does not require an understanding on a molecular level of what exactly takes place during a claimed process. The EA is long on argumentation, while it is utterly devoid of any probative evidentiary submission. and the EA even fails to support its speculative, postulative assertions with the examiner's declaration as required under the rules. In contrast, the applicants' evidence in the disclosure about the demonstrated fact of the absence of hydrogen cyanide during the claimed reaction, which was filed with their declaration, factually contradicts the examiner's speculative assertions.

(d) The EA misrepresents the reference. It actually teaches away from the herein claimed single step reaction when the reference maintains that acetic acid alone is not strong enough to form cyanic acid from its salts.

(e) The EA also misrepresents the claims on appeal as not having been changed from those that were involved in the earlier appeal, however, the fact is that the claims were seriously restricted since then to the single acid (acetic acid) which the reference stated that it cannot use in its process.

(B) Reply to the Examiner's Answer

The examiner's statement (10) is in error as he mischaracterizes the applicants' invention in his summary of the invention. The correct statement of the invention on page 5 of the Examiner's Answer reads: "Applicants [sic] process is summarized in the following reaction scheme: They employ a mixture of sodium cyanate in acetic acid to convert iminostilbene to Carbamazepine."

The foregoing correct statement of the applicants' claimed single step process is followed by the examiner's **erroneous** non-sequitur, in the penultimate sentence on the page which reads: "The sodium cyanate and acetic acid are reacted to form cyanic acid." That is definitely **not** the applicants' process, and the sole reference Acklin et al. expressly teaches that acetic acid is too weak an acid to be able to liberate cyanic acid from its salts, such as the sodium cyanate[1]. The examiner is further in error, at

[1] The paragraph in column 2, lines 39-54 of Acklin et al. reads (in translation) "For liberating of cyanic acid from one of its salts ... generally several protonic acids which have a sufficient acid strength, are suitable ... . Suitable are, for example, mineral acids, such as hydrochloric acid, or sulfuric acid, or organic sulfonic acids ... or organic carbonic acids the acid strength of which in the solvent that is employed is practically that of formic acid, such as 2-mono-, 2,2-di-, or 2,2,2,-trihalogen-C_2-C_7-alkane acids, e.g. trichloroacetic acid."

least in part, when he goes on on page 5 "In the present claims acetic acid is part of all solvent choices ... " in that in addition to acetic acid, **only** alcohol and water may be present to the extent as alcohol and water may be viewed as solvents in this case.

The examiner's erroneous and speculative attribution of the reaction scheme at the bottom on page 5 of the Examiner's Answer, and his speculative statement in the quote above that acetic acid liberates cyanic acid from its salts (something that the sole reference teaches cannot take place), was **repeatedly** challenged in these proceedings, and his declaration in support of his contradiction of the teachings of the sole reference Acklin et al. pursuant to 37 C.F.R. 104(d)(2) was repeatedly requested, and was entirely ignored so far by the examiner.

The examiner's statements on page 6, with respect to the previous PTO translation error, are correct, but only up to the end of the first sentence of the second paragraph on page 7. The examiner, however, is **entirely wrong** when he rejects the present claims over claim 14 of claim 14 of Acklin et al., because claim 14 of Acklin et al. is directed to the reaction of cyanic acid and iminostilbene, whereas in the present claims that reaction does not occur. In contrast, in the present claims there is no cyanic acid, but the reaction takes place between carbamazepine and **sodium cyanate** instead. This is the "small detail" which the examiner always glosses over with his speculative assertions about what "a process chemist would realize," which assertions are not supported by any evidence that is required, such as a reference or a declaration pursuant to 37 C.F.R. 1.104(d)(2).

Claim 14 of the reference does, indeed, use acetic acid concurrently as a solvent and an acidic catalyst, but **not to liberate cyanic acid from its salts (i.e. sodium cyanate)**. The reference teaches that particular reaction requires a stronger acid than acetic acid, i.e."an acid at least as strong as formic acid." But claim 14 of the sole reference, as pointed out above, does not relate to the reaction that is carried out in accordance with the claims on appeal herein, but it relates to a reaction between entirely different reaction partners, namely cyanic acid and iminostilbene, and it has been well established by various properties of the herein claimed reaction the cyanic acid is not being used in the herein claimed reactions.

The examiner is also wrong in his speculative attribution on page 7, of what a process chemist "would realize" when stating on page 7, "that the reference possessed the concept of generating the cyanic acid from its salt." Yes, Acklin et al. **does** liberate cyanic acid from its salts, but that step is the first step of its two-step reaction, and that first step cannot be carried out with acetic acid, but requires that stronger acid. That first step is not claimed in claim 14 of Acklin et al., but it is claim 5 of that reference which sets forth the first process step of Acklin et al. the manner in which the cyanic acid is obtained, which initial reaction product is then further reacted in claim 14. The second step of Acklin et al., which is set forth in claim 14, does not

employ, and does not require any other acid than acetic acid, but that is an entirely different reaction than is claimed herein. The examiner's misplaced emphasis on the word "concurrently" in actualithy refers to the reaction solely of claim 14, in that acetic acid is used "*gleichzeitig* [i.e. at the same time], as solvent and acidic agent." Thus the word *gleichzeitig* (concurrently, or at the same time), in spite of the examiner's distorted translational attribution, does **definitely not** relate to being "the agent to react with sodium cyanate ... to generate cyanic acid."

In fact, the none of examples 1-3 of the reference to which the examiner refers for support use acetic acid, or aqueous acetic acid, or alcoholic acetic acid. All of those examples do not support the examiner, as Example 1 uses 723 g **trichloro**acetic acid (about ½ the PkA of acetic acid, i.e. even stronger than formic acid) dissolved in 600 ml toluene reacted with a toluene solution of iminostilbene and sodium cyanate both in toluene; Example 2 uses iminostilbene, suspended in acetic acid, sodium cyanate **and sulfuric acid**; and Example 3 uses sodium cyanate with **acetic acid ethylester and hydrochloric acid.**

To repeat, because the examiner continues to repeat himself, claim 14 **does** teach use of acetic acid as the sole acidic agent, but claim 14 does not relate to the reaction that is claimed herein namely iminostilbene with a cyanate salt. The forming of cyanic acid, one of the reactants of claim 14, is carried out in another process step by Acklin et al., that other process step being separate from claim 14, and needs to employ the stronger acid.

Example 2 of Acklin et al. does teach a process of adding sodium cyanate to iminostilbene, but the examiner misstates the disclosure of Example 2 of Acklin et al, because that Example **does not use any acetic acid**. Example 2 of Acklin et al. employs **trichloro**acetic acid, i.e. an acid that is more than twice as strong an acid as acetic acid.

The examiner is **also wrong** when he states that the claims were not narrowed since the previous appeal. In fact, the claims were amended to recite that the acidic medium "**consists of**" acetic acid, or diluted versions thereof. It is that essential restriction which is at the heart of this appeal and is entirely glossed over by the examiner.

Although the further claims do not require further arguments, since they all depend from claim 8 (which was argued in favor of *ad nauseam*), and independent claim 9 was stated to be allowable, the examiner's reference to Examples 9 and 10 of Acklin et al. suffers from the same conceptual confusion as all of the other rejections discussed hereinabove. Yes, Examples 9 and 10 of Acklin et al. do use acetic acid as the sole acid, but in those examples only the second reaction step of Acklin et al. is carried out, because in both examples the separately prepared cyanic acid is reacted

with iminostilbene, i.e. solely the reaction step of claim 14 which is not done in the presently claimed process.

The text of Acklin et al. referred to by the examiner (column 1, line 54, to column 2, line 16) deals only with: (i) the reaction between iminostilbene with cyanic acid, i.e. the second process step of claim 14 (col 1, lines 55-62); (ii) state that (i) can take place in the presence of an "acidic accelerating agent" (i.e. an acidic catalyst in "catalytic amounts")(column 2, line 62 to column 3, line 6); and (iii) not to use too much of that acid, because in the case of multibasic acids and their clearly different acidity levels in the case of heterogenous reactions acid salts can precipitate by which a part of the employed acid will be blocked (column 3, lines 6-14). There is nothing else stated in that part of Acklin et al. to which the examiner refers and, in fact, in column 1, line 55 even to the end of the paragraph in column 2, in line 26, **acetic acid is nowhere even alluded to,** and, of course that entire discussion and the examiner's comments deal with claim 14 (and Examples 9 and 10 of Acklin et al.), which is an entirely different process than that which is claimed herein, and also different from Acklin's first reaction step.

Further to the examiner's unsupported speculation of what is "chemically reasonable" entirely contradicts the teaching of Acklin et al. which requires an acid that is stronger than acetic acid (an acid at least as strong as formic acid) to liberate cyanic acid from its salts, and the examiner has entirely failed to provide any evidence, other than his theoretical speculation in support. It is not the applicants, but the reference which asserted that a stronger acid than acetic acid is required to liberate cyanic acid from its salts. Contradiction of the teaching of the reference requires support, i.e. evidence rather than unsupported speculative argumentation than the examiner's mere speculation and failure even to supply a declaration under 37 C.F.R.1.104(d)(2). The chemical books late-cited, but not even supplied for the first time in this Examiner's Answer do not constitute evidence in the absence of the demanded declaration to link them together. As has also been amply supported in the application itself that cyanic acid is a foul smelling, highly toxic gas which requires it to be carried out under protection, whereas the one-step process of the present invention (with excellent yield, one might add) does not require any protection, and there is no evidence of any cyanic acid formation, further supporting that the examiner's speculation is entirely incorrect.

The unsupported speculation about "trimolecular complex," and "collision among three molecules" and "diffusion-limited proton transfer process" as violating the laws of chemistry, has no evidentiary support and is not probative of anything. I don't know how these unwarranted speculations that are vastly removed from reality and even contradict the teachings of the reference, can actually impress anyone with anything.

The examiner's speculation is further suspect and contrary to practical experience for the reason that he states that in comparison with the "practically

instantaneous" reaction between acetic acid and the cyanate salt (which Acklin et al. teaches cannot even take place), is followed by the slower subsequent reaction between the cyanic acid with iminostilbene. If that were the case, copious amounts of the toxic, foul smelling cyanic acid would linger around, whereas we know for a fact that this is not the case.

(C) Conclusion

The examiner's continued, repetitive reliance on the process of claim 14 is tiresome, because it continues to ignore the fact that claim 14 is directed to a different process between different reaction partners than is claimed herein. In view of the examiner's confusion of what is taught by Acklin et al., and his continued speculative maintenance of teachings contrary to the reference, coupled with his failure to offer any evidentiary support for his own speculations, all of these facts counsel to the Board declining to receive further oral argumentation from the examiner in the frame of an oral hearing.

Please note the undersigned attorney's new address as it appears below.

Respectfully submitted

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